REMARKS

Claims 1, 3-5, 7–14, 17, 20, and 21-41 are pending in this application. Claims 1, 21, 31, and 41 are the independent claims, and are amended herein. For the foregoing reasons, all of the pending claims should be allowed.

The Cited References Do Not Show All Elements Of The Pending Claims

Even if combined as suggested by the Examiner, the cited references do not describe or suggest each element of the pending claims. For instance, none of the references show a metallic insert comprising at least two separate metallic parts, the first part being removable from the irradiation cell without removal of the second party by sliding the first part in a direction parallel to the particle beam. BE 1011263 shows only a one-piece unitary insert that lacks a first part and second part that are separately removable. Zeisler does not show a removable insert, and neither the copper ring nor the niobium sphere that are bolted together can be removed from other portions of the device by sliding in a direction parallel to the particle beam. Further, none of the references describe an insert comprising at least a first part machined from niobium or tantalum as in claims 21 and 41. BE 1011263 does not disclose these materials, and Zeisler shows only a niobium sphere made from two niobium foils stamped to form hemispheres and welded together, not a machined part. The references also fail to describe the wall thicknesses of claims 1 and 41.

More particularly, it is apparent from the response to Applicant's arguments that the Examiner has taken a broad reading of the term "separate." Claims 1, 21, 31, and 41 have each been amended to clarify that the first insert part (which forms the cavity) is removable from the irradiation cell without removal of the second part by sliding the first part in a direction parallel to the particle beam. Thus the first and second portions of the insert must be both separate and separable so that the first

insert part can be removed without also removing the second insert part. Thus, the first insert part may be easily replaced without the need to replace the entire insert device. The cited references, including BE 1011263, Zeisler et al., and 6,586,747 to Erdman, all completely fail to show such an insert with two parts that may be separated.

Claims 1 and 41 also have been amended to describe a particular wall thickness (0.3 to 0.7 mm) of the portion of the first insert part that surrounds the cavity. As discussed in paragraph [0039] of the present application, Applicants have surprisingly found that a thickness of about 0.3 mm to about 0.7 mm, preferably about 0.5 mm, provides acceptable heat exchange and maintains sufficient strength to support high internal pressure in the cavity, while avoiding porosity problems that could arise due to the nature of the material used (for instance, niobium). BE 1011263 does not describe an insert having this wall thickness, and indeed as discussed at length in prior amendments it would not be possible to machine an insert as shown in BE 1011263 out of niobium to have a thickness of 0.3-0.7 mm surrounding the target cavity. The Zeisler reference also fails to describe or suggest an insert part having such thickness, especially from niobium. The target sphere in Zeisler is described as formed from welding together two hemispheres 0.25 mm thick, but also could have been thinner since it was estimated to be capable of withstanding a pressure of 253 bar (p. 451), but the level of irradiation used never resulted in pressure greater than 12 bar (see p. 451, Fig. 3). Therefore, Zeisler would not have suggested to one of ordinary skill in the art that BE 1011263 should be modified to have a two-part insert with the first part having a wall thickness of 0.3-0.7 mm surrounding the target cavity as in independent claims 1 and 41.

Claims 21 and 41 further describe the first insert part as being machined from a material selected from the group consisting of niobium and tantalum. In Zeisler, the target sphere is formed by a much different process. BE 1011263 does not disclose the

use of parts machined from niobium or tantalum. The Zeisler spherical niobium target has no irradiation window, i.e. the beam directly traverses the target chamber wall. The authors built the sphere from two niobium hemispheres formed with a hydraulic press, and then later electron-beam welded the hemispheres together. The authors also drilled holes in the centers of the hemispheres and electron-beam welded niobium tubes to the holes. The welding of the parts creates a target that is less suitable than one machined from a solid bock of niobium, because the welded target will be brittle and less able to withstand pressure. The target would also contain many uneven points or asperities where a non negligible amount of the irradiated target can be adsorbed.

<u>The Cited References Would Not Be Combined By A Person Having Ordinary Skill In The Art</u>

One of ordinary skill in the art would not have modified the insert of BE '263 in view of Zeisler. Zeisler describes a spherical target chamber that is substantially different than the insert design of BE '263 and lacks an elongate target cavity. Zeisler does not at all suggest how one would modify the complex structure of the insert of BE '263 in order to utilize the material properties of niobium while also maintaining the beneficial structural features of the '263 insert. Zeisler does not show any parts machined from Niobium, and therefore the welded sphere of Zeisler would not suggest a modification of the materials of the much different target chamber of BE '263. Combining the Zeisler article with BE '263 would suggest only replacing a one-piece silver or titanium insert with a spherical niobium insert, but would not suggest to one of ordinary skill in the art a two-part insert made of two different materials. As pointed out in the previously submitted declaration under 37 C.F.R. 1.132, niobium, tantalum, and other similar materials are difficult to machine, and one of ordinary skill

would not have believed that niobium or tantalum was an appropriate material for manufacturing the complex target chamber insert of BE '263.

One of ordinary skill in the art also would not have modified the insert of BE '263 in view of the integral holder body and rear window of Erdman '747 that are made of niobium. The target chamber and rear window of Erdman '747 are made from a solid block of niobium, and there is no suggestion that the advantages of the present application may be achieved by replacing the one-piece insert of BE '263 with a two-piece insert.

There has been no meaningful articulated reason why applicant or a person of ordinary skill would use very particular aspects of Zeisler (or Erdman, for that matter) to modify the BE '263 and arrive at the invention described in the claims (even if the combined teachings showed every element of the claims, which they do not). *Ex parte Whalen*, 89 U.S.P.Q.2d 1078 (BPAI 2008); Ex parte Alexander, 86 U.S.P.Q. 2d 1120, 1123 (BPAI 2007). The Board in *Whalen* stated:

> The U.S. Supreme Court recently held that rigid and mandatory application of the "teaching-suggestion-motivation," or TSM, test is incompatible with its precedents. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 [82 USPQ2d 1385] (2007). The Court did not, however, discard the TSM test completely; it noted that its precedents show that an invention "composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.*
>
> The Court held that the TSM test must be applied flexibly, and take into account a number of factors "in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed." *Id.* at 1740-41. Despite this flexibility, however, the Court stated that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements in the way the claimed new invention does." *Id.* "To facilitate review, this analysis should be made explicit." *Id.*"
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> The KSR Court noted that obviousness cannot be proven merely by showing that the elements of a claimed device were known in the

> prior art; it must be shown that those of ordinary skill in the art would have has some "apparent reason to combine the known elements in the fashion claimed." *Id*. at 1741.
>
> In the same way, when the prior art teaches away from the claimed solution as presented here (FF12, FF20, FF22 and FF 24), obviousness cannot be proven merely by showing that a known composition could have been modified by routine experimentation or solely on the expectation of success; it must be shown that those of ordinary skill in the art would have had some apparent reason to modify the known composition in a way that would result in the claimed composition.

Further distinctions over each of the cited references are discussed below.

The Problem And Applicants' Solution

As explained in the Background section of the present application, the choice of insert material in irradiation cell target chambers is particularly important. It is necessary to avoid the production of radioisotopes that disintegrate by high-energy gamma particle emission and make any mechanical intervention on the target difficult due to radiosafety problems, while also providing for adequate heat dissipation. In addition, machinability is also an important consideration for the insert material, particularly where the insert is of a complex structure.

Many prior art references disclosing irradiation cells do not utilize an insert (i.e. a separate part comprising the cavity that is introduced into the irradiation cell), but rather comprise several parts assembled together without the ability to easily insert and remove the target chamber and surrounding elements. (Application ¶26). These prior art irradiation cells lack many of the advantages of devices described in the present application and BE '263, which was cited by the Examiner.

The References

<u>BE '263 describes a target chamber, but does not use niobium and discloses only a one piece insert.</u>

BE '263 describes a one piece insert made of silver or titanium, not niobium or tantalum. The Examiner has indicated that the unitary insert may be viewed as having two or more separate parts. However, even from this perspective, BE '263 does not disclose or suggest a two-part insert wherein a first insert part (which forms the cavity) is removable from the irradiation cell without removal of a second insert part by sliding the first part in a direction parallel to the particle beam.

Further, although it would be beneficial to use niobium or tantalum for a target chamber insert, niobium and tantalum are difficult to machine and therefore are difficult materials to use for making an insert of complex design, such as the insert described in BE '263. (Application ¶23). For example, a built up edge may occur on the tools used to machine the niobium, leading to high tool wear and/or breakage, and the use of electrical discharge machining is not effective. (Id.). Therefore, one of ordinary skill in the art would not have believed that the complex insert of BE '263 could be made of niobium or tantalum as described in claims 21 and 41.

The claims of the present application recite an irradiation cell that has a removable insert comprising two insert parts, each of the insert parts being made of different materials. This two-part insert design allows for inserts with longer cavities and improved heat exchange, while allowing the insert to be as chemically inert as possible. Using this two-part design, for instance, a target cavity may have a first part with an overall length of 50mm or greater even when made of difficult to machine materials such as niobium or tantalum. (Application ¶36). A cavity of such increased length has improved heat exchange, and can improve irradiation efficiency with gaseous targets by providing a longer distance over which target vapor can react with a proton beam. (Application ¶39). Without the two part design of the present

application, even a similar device, such as described in BE '263, could not achieve the foregoing advantages.

Further, BE '263 discloses a one-piece insert made of solid silver or titanium. Replacing the one-piece insert of the prior art with a two-part insert comprised of two different materials would not be obvious as argued by the Examiner. The claimed two-part insert with a removable part as described in all of the claims surprisingly allows the cavity of the insert to be significantly longer than in the prior art, increasing efficiency and heat exchange properties. (Application ¶39). This is not simply a case of replacing a one-piece device with a two-piece device having identical properties, and therefore the reasons for obviousness argued by the Examiner do not apply in this instance.

There is no suggestion in the art of record that the insert of BE '263 may be made with two distinct parts so that a different material may be used for each part. In fact, although it would be beneficial to use niobium or tantalum for a target chamber insert, niobium is difficult to machine and therefore a difficult material to use for making an insert of complex design, such as the insert described in BE '263. (Application ¶23). A built up edge may occur on the tools used to machine the niobium, leading to high tool wear and/or breakage, and the use of electrical discharge machining is not effective. (Id.). Therefore, one of ordinary skill in the art at the time of the filing of this application would not have believed that the complex insert of BE '263 could be made of niobium or tantalum, as described in claims 21 and 41.

<u>The Zeisler Technical Note Discloses Only A One-Piece Target Chamber Made Of A Single Material (Niobium), And Does Not Suggest Using Two Or More Materials. Therefore, At Most Zeisler Suggests Replacing The Entire Insert Of BE 1011263 With Niobium, Yielding A One-Piece Niobium Insert.</u>

The Examiner argues that it would be obvious to combine BE '263 with a technical note written by Zeisler et al. ("Zeisler"), which discusses the use of niobium to construct a target chamber. However, the structure of Zeisler is substantially different than the structure of BE '263 and other devices, and one of ordinary skill would not have combined structural aspects of Zeisler and the complex insert of BE '263. The device described by Zeisler is shown below:

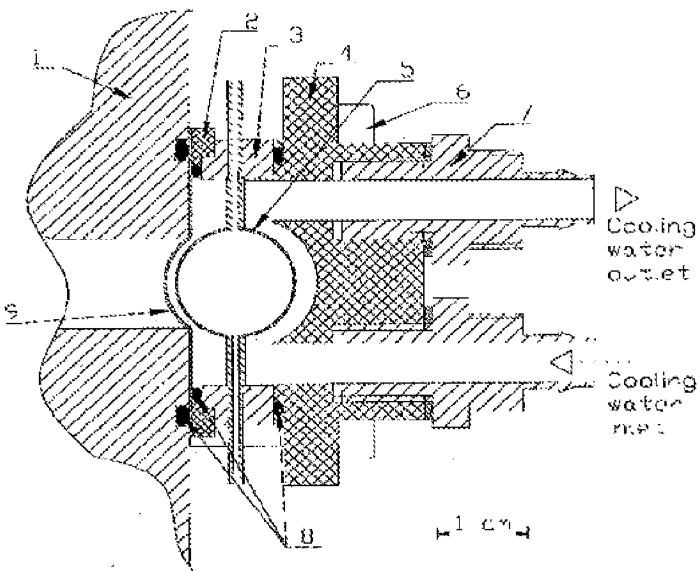

Fig. 2. Simplified technical drawing of the target system. (1) collimator (aluminum); (2) spacer (PEEK®); (3) holder ring (copper); (4) back plate (PEEK®); (5) target chamber (niobium); (6) bolt (SS 316, M 4); (7) fitting (SS 316, 5 mm i.d.); (8) O-rings (Viton®); (9) vacuum window (aluminum, 0.3 mm thickness).

The target chamber does not include an elongate target cavity machined from niobium, and is instead formed by welding two hemispheres of niobium to form a spherical cavity. The manner in which the target is formed thus leads to certain structural disadvantages, including weak points attributable to the welding process. The Zeisler target chamber is also does not have a cavity closed by a window, as required by the claims, but instead is fully enclosed by the two niobium hemispheres. However, as discussed above, niobium, tantalum, and other similar materials are

difficult to machine, and one of ordinary skill would not have believed that niobium or tantalum was an appropriate material for manufacturing the complex target chamber insert of BE '263.

Even though Zeisler discloses certain benefits of niobium target chambers, it does not disclose inserts made of both niobium and another metal such as silver or titanium. The target described is made from two niobium hemispheres and a niobium tube welded together to form a unitary structure. (Zeisler p. 450). The target chamber is shown in Figs. 1 and 2 and is simply referred to as a niobium target chamber. This niobium target chamber is discussed only as a replacement for silver or titanium target chambers, not as being used in combination with silver or titanium target chamber parts. (Zeisler pp. 449, 450). The target chamber is assembled with a copper ring and other components of the irradiation cell so that water may surround the front of the spherical target chamber. (Zeisler p. 450).

The spherical target chamber of Zeisler is substantially different than the insert design of BE '263, and suggests only that niobium is a suitable material for a target chamber. Zeisler does not, for instance, show an elongate target chamber that is longer in the direction of the particle beam. Nor does Zeisler show a first insert part (which forms the cavity) that is removable from the irradiation cell without removal of a second part by sliding the first part in a direction parallel to the particle beam. The components of Zeisler are welded together and could not be easily separated from the outer copper ring to which they are bolted. Zeisler also would not suggest to one of ordinary skill in the art machining an elongate target cavity from niobium. Zeisler does not at all suggest how one would modify the complex structure of the insert of BE '263 in order to utilize the material properties of niobium while also maintaining the beneficial structural features of the '263 insert. Combining the Zeisler article with BE '263 would suggest at most replacing a one-piece silver or titanium insert with a

niobium insert, but would not suggest to one of ordinary skill in the art a two-part insert made of two different materials.

Erdman 6,586,747 Does Not Disclose A Two-Piece Insert, Does Not Disclose An Insert Made Up Of Two Different Metallic Materials, And Would Not Have Been Combined With BE '263

Although the Office Action indicates that rejections based on Erdman have been withdrawn, that reference is still mentioned in the rejections based on 35 U.S.C. 103. Therefore, a short discussion of the reasons why Erdman does not render the claimed invention obvious is set forth below. Additional distinctions over Erdman were described in Applicants' previous amendment.

Erdman '747 does not does not describe an irradiation cell with an insert, but rather describes a series of parts assembled together to form an irradiation cell, as shown below. The target cavity 60 of Erdman is wide and shallow, and disposed at an oblique angle relative to the direction of the proton beam within a holder body Erdman does not disclose a first part 64 made of niobium and a second part 56 made of silver. Instead, the holder body and rear window are *integrally formed*. (Erdman col. 5 lns 57-63). The target cavity 60 is machined into one side of the holder body, leaving a thin rear window 64 at the end of the target cavity. (Id.). The holder body 56 of

Erdman '747 identifies its holder body, which includes the target cavity and rear window, as an alternative to prior art silver target holders that contain impurities and are therefore less advantageous. (Erdman col. 2 lns 41-63; col. 6 lns 14-33). While Erdman acknowledges that other *chemically inert* materials may be used instead of niobium (col. 6 lns 14-33), it specifically teaches away from the use of silver holder bodies. Therefore, Erdman does not disclose the use of a combination of niobium and silver, but rather describes niobium and silver as alternatives to one another.

The structure of the Erdman target cavity is substantially different than that of BE '263 and the structure described in the claims of the present application. Erdman shows a shallow target cavity, and increasing the length of the target cavity is undesirable, as it increases the volume of the target cavity and may therefore become economically undesirable by requiring more initial liquid target material. (Erdman col. 6 lns 61-67). Therefore, one of ordinary skill in the art would not have applied the disclosure of Erdman to irradiation cell designs with longer target cavities, such as BE '263.

<u>The Claims Are Not Obvious-The References Alone Or In Combination Do Not Suggest A Two Piece Insert</u>

As explained above and in the Declaration of Jean-Claude Amelia previously submitted, none of the cited prior art discloses or suggests a two-part insert, let alone a two-part insert made of two different materials. As the present application indicates, silver and titanium have properties that in some respects are more advantageous than those of niobium in the construction of metallic inserts for target chambers. For instance, silver and titanium are easier to machine than niobium or tantalum and have better thermal conductivity. On the other hand, niobium and tantalum have very low chemical reactivity and are therefore beneficial materials for irradiation targets. Without a two-part insert as claimed herein, the cavity for holding the target material cannot have the overall length and heat exchange properties desired while still having the chemical inertness of niobium or tantalum Therefore, the claimed two-part insert has advantages lacking in both the prior art BE '263 patent and the Zeisler technical note. None of the prior art suggests a two-part insert with the same advantages.

One of ordinary skill in the art would not have modified the insert of BE '263 in view of Zeisler. Zeisler describes a spherical target chamber that is substantially different than the insert design of BE '263 and lacks an elongate target cavity, and

suggests only that niobium is a suitable material for a target chamber. Zeisler does not at all suggest how one would modify the complex structure of the insert of BE '263 in order to utilize the material properties of niobium while also maintaining the beneficial structural features of the '263 insert. Combining the Zeisler article with BE '263 would suggest only replacing a one-piece (unitary) silver or titanium insert with a niobium insert, but would not suggest to one of ordinary skill in the art a two-part insert made of two different materials.

One of ordinary skill in the art would also not have modified the insert of BE '263 in view of the integral holder body and rear window of Erdman '747 that are made of niobium. The target chamber and rear window of Erdman '747 are machined from a solid block of niobium, and there is no suggestion that the advantages of the present application may be achieved by replacing the one-piece insert of BE '263 with a two-piece insert.

Conclusion

For the foregoing reasons, it is respectfully requested that claims 1, 3-5, 7–14, 17, 20, and 21-41 be allowed to pass to issue.

The Commissioner is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 06-1135.

Respectfully submitted,

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